#6

```
                    RAW SEQUENCE LISTING              DATE: 10/30/2001
                    PATENT APPLICATION:  US/09/903,248  TIME: 15:16:58

                    Input Set : A:\Rih32d51.app
                    Output Set: N:\CRF3\10302001\I903248.raw

      3 <110> APPLICANT: Wands, Jack R.
      4        de la Monte, Suzanne M.
      5        Ince, Nedim
      6        Carlson, Rolf I.
      8 <120> TITLE OF INVENTION: DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS
     10 <130> FILE REFERENCE: 21486-032 DIV5
     12 <140> CURRENT APPLICATION NUMBER: 09/903,248
     13 <141> CURRENT FILING DATE: 2001-07-11
     15 <150> PRIOR APPLICATION NUMBER: 09/436,184
     16 <151> PRIOR FILING DATE: 1999-11-08
     18 <160> NUMBER OF SEQ ID NOS: 9
     20 <170> SOFTWARE: PatentIn Ver. 2.1
     22 <210> SEQ ID NO: 1
     23 <211> LENGTH: 36
     24 <212> TYPE: PRT
     25 <213> ORGANISM: Artificial Sequence
     27 <220> FEATURE:
     28 <223> OTHER INFORMATION: Description of Artificial Sequence: Consensus
     29        EGF-like domain
     31 <220> FEATURE:
     32 <221> NAME/KEY: VARIANT
     33 <222> LOCATION: (2)..(8)
     34 <223> OTHER INFORMATION: Wherein Xaa is any amino acid
     36 <220> FEATURE:
     37 <221> NAME/KEY: VARIANT
     38 <222> LOCATION: (10)..(13)
     39 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     41 <220> FEATURE:
     42 <221> NAME/KEY: VARIANT
     43 <222> LOCATION: (15)..(24)
     44 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     46 <220> FEATURE:
     47 <221> NAME/KEY: VARIANT
     48 <222> LOCATION: (26)
     49 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
     51 <220> FEATURE:
     52 <221> NAME/KEY: VARIANT
     53 <222> LOCATION: (28)..(35)
     54 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
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     58 1               5                   10                  15
W--> 60 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Cys Xaa Xaa Xaa Xaa Xaa
     61             20          25                  30
W--> 63 Xaa Xaa Xaa Cys
     64         35
     67 <210> SEQ ID NO: 2
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ENTERED

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70 <213> ORGANISM: Homo sapiens
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76 Gly Ser Gly Ser Gly Ser Thr Ser Ala Gly Ser Ser Ser Pro Gly Ala
77              20                  25                  30
79 Arg Arg Glu Thr Lys His Gly Gly His Lys Asn Gly Arg Lys Gly Gly
80          35                  40                  45
82 Leu Ser Gly Thr Ser Phe Phe Thr Trp Phe Met Val Ile Ala Leu Leu
83      50                  55                  60
85 Gly Val Trp Thr Ser Val Ala Val Val Trp Phe Asp Leu Val Asp Tyr
86  65                  70                  75                  80
88 Glu Glu Val Leu Gly Lys Leu Gly Ile Tyr Asp Ala Asp Gly Asp Gly
89              85                  90                  95
91 Asp Phe Asp Val Asp Asp Ala Lys Val Leu Leu Gly Leu Lys Glu Arg
92              100                 105                 110
94 Ser Thr Ser Glu Pro Ala Val Pro Pro Glu Glu Ala Glu Pro His Thr
95          115                 120                 125
97 Glu Pro Glu Glu Gln Val Pro Val Glu Ala Glu Pro Gln Asn Ile Glu
98      130                 135                 140
100 Asp Glu Ala Lys Glu Gln Ile Gln Ser Leu Leu His Glu Met Val His
101 145                 150                 155                 160
103 Ala Glu His Val Glu Gly Glu Asp Leu Gln Gln Glu Asp Gly Pro Thr
104              165                 170                 175
106 Gly Glu Pro Gln Gln Glu Asp Asp Glu Phe Leu Met Ala Thr Asp Val
107              180                 185                 190
109 Asp Asp Arg Phe Glu Thr Leu Glu Pro Glu Val Ser His Glu Glu Thr
110          195                 200                 205
112 Glu His Ser Tyr His Val Glu Glu Thr Val Ser Gln Asp Cys Asn Gln
113      210                 215                 220
115 Asp Met Glu Glu Met Met Ser Glu Gln Glu Asn Pro Asp Ser Ser Glu
116 225                 230                 235                 240
118 Pro Val Val Glu Asp Glu Arg Leu His His Asp Thr Asp Asp Val Thr
119              245                 250                 255
121 Tyr Gln Val Tyr Glu Glu Gln Ala Val Tyr Glu Pro Leu Glu Asn Glu
122          260                 265                 270
124 Gly Ile Glu Ile Thr Glu Val Thr Ala Pro Pro Glu Asp Asn Pro Val
125          275                 280                 285
127 Glu Asp Ser Gln Val Ile Val Glu Glu Val Ser Ile Phe Pro Val Glu
128      290                 295                 300
130 Glu Gln Gln Glu Val Pro Pro Glu Thr Asn Arg Lys Thr Asp Asp Pro
131 305                 310                 315                 320
133 Glu Gln Lys Ala Lys Val Lys Lys Lys Pro Lys Leu Leu Asn Lys
134              325                 330                 335
136 Phe Asp Lys Thr Ile Lys Ala Glu Leu Asp Ala Ala Glu Lys Leu Arg
137          340                 345                 350
139 Lys Arg Gly Lys Ile Glu Glu Ala Val Asn Ala Phe Lys Glu Leu Val
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RAW SEQUENCE LISTING   DATE: 10/30/2001
PATENT APPLICATION: US/09/903,248   TIME: 15:16:58

Input Set : A:\Rih32d51.app
Output Set: N:\CRF3\10302001\I903248.raw

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140          355                    360                    365
142 Arg Lys Tyr Pro Gln Ser Pro Arg Ala Arg Tyr Gly Lys Ala Gln Cys
143       370                    375                    380
145 Glu Asp Asp Leu Ala Glu Lys Arg Arg Ser Asn Glu Val Leu Arg Gly
146 385                    390                    395                    400
148 Ala Ile Glu Thr Tyr Gln Glu Val Ala Ser Leu Pro Asp Val Pro Ala
149                    405                    410                    415
151 Asp Leu Leu Lys Leu Ser Leu Lys Arg Arg Ser Asp Arg Gln Gln Phe
152                    420                    425                    430
154 Leu Gly His Met Arg Gly Ser Leu Leu Thr Leu Gln Arg Leu Val Gln
155           435                    440                    445
157 Leu Phe Pro Asn Asp Thr Ser Leu Lys Asn Asp Leu Gly Val Gly Tyr
158       450                    455                    460
160 Leu Leu Ile Gly Asp Asn Asp Asn Ala Lys Lys Val Tyr Glu Glu Val
161 465                    470                    475                    480
163 Leu Ser Val Thr Pro Asn Asp Gly Phe Ala Lys Val His Tyr Gly Phe
164                    485                    490                    495
166 Ile Leu Lys Ala Gln Asn Lys Ile Ala Glu Ser Ile Pro Tyr Leu Lys
167           500                    505                    510
169 Glu Gly Ile Glu Ser Gly Asp Pro Gly Thr Asp Asp Gly Arg Phe Tyr
170       515                    520                    525
172 Phe His Leu Gly Asp Ala Met Gln Arg Val Gly Asn Lys Glu Ala Tyr
173       530                    535                    540
175 Lys Trp Tyr Glu Leu Gly His Lys Arg Gly His Phe Ala Ser Val Trp
176 545                    550                    555                    560
178 Gln Arg Ser Leu Tyr Asn Val Asn Gly Leu Lys Ala Gln Pro Trp Trp
179                    565                    570                    575
181 Thr Pro Lys Glu Thr Gly Tyr Thr Glu Leu Val Lys Ser Leu Glu Arg
182       580                    585                    590
184 Asn Trp Lys Leu Ile Arg Asp Glu Gly Leu Ala Val Met Asp Lys Ala
185       595                    600                    605
187 Lys Gly Leu Phe Leu Pro Glu Asp Glu Asn Leu Arg Glu Lys Gly Asp
188       610                    615                    620
190 Trp Ser Gln Phe Thr Leu Trp Gln Gln Gly Arg Arg Asn Glu Asn Ala
191 625                    630                    635                    640
193 Cys Lys Gly Ala Pro Lys Thr Cys Thr Leu Leu Glu Lys Phe Pro Glu
194                    645                    650                    655
196 Thr Thr Gly Cys Arg Arg Gly Gln Ile Lys Tyr Ser Ile Met His Pro
197           660                    665                    670
199 Gly Thr His Val Trp Pro His Thr Gly Pro Thr Asn Cys Arg Leu Arg
200       675                    680                    685
202 Met His Leu Gly Leu Val Ile Pro Lys Glu Gly Cys Lys Ile Arg Cys
203       690                    695                    700
205 Ala Asn Glu Thr Arg Thr Trp Glu Glu Gly Lys Val Leu Ile Phe Asp
206 705                    710                    715                    720
208 Asp Ser Phe Glu His Glu Val Trp Gln Asp Ala Ser Ser Phe Arg Leu
209                    725                    730                    735
211 Ile Phe Ile Val Asp Val Trp His Pro Glu Leu Thr Pro Gln Gln Arg
212                    740                    745                    750
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214 Arg Ser Leu Pro Ala Ile
215          755
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219 <211> LENGTH: 2324
220 <212> TYPE: DNA
221 <213> ORGANISM: Homo sapiens
223 <400> SEQUENCE: 3
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225 gctccggcag cggtagcacg agtgcgggca gcagcagccc cggggcccgg agagagacaa 120
226 agcatggagg acacaagaat gggaggaaag gcggactctc gggaacttca ttcttcacgt 180
227 ggtttatggt gattgcattg ctgggcgtct ggacatctgt agctgtcgtt tggtttgatc 240
228 ttgttgacta tgaggaagtt ctaggaaaac taggaatcta tgatgctgat ggtgatggag 300
229 attttgatgt ggatgatgcc aaagttttat taggacttaa agagagatct acttcagagc 360
230 cagcagtccc gccagaagag gctgagccac acactgagcc cgaggagcag gttcctgtgg 420
231 aggcagaacc ccagaatatc gaagatgaag caaaagaaca aattcagtcc cttctccatg 480
232 aaatggtaca cgcagaacat gttgagggag aagacttgca acaagaagat ggacccacag 540
233 gagaaccaca acaagaggat gatgagtttc ttatggcgac tgatgtagat gatagatttg 600
234 agaccctgga acctgaagta tctcatgaag aaaccgagca tagttaccac gtggaagaga 660
235 cagtttcaca agactgtaat caggatatgg aagagatgat gtctgagcag gaaaatccag 720
236 attccagtga accagtagta gaagatgaaa gattgcacca tgatacagat gatgtaacat 780
237 accaagtcta tgaggaacaa gcagtatatg aacctctaga aaatgaaggg atagaaatca 840
238 cagaagtaac tgctccccct gaggataatc ctgtagaaga ttcacaggta attgtagaag 900
239 aagtaagcat ttttcctgtg gaagaacagc aggaagtacc accagaaaca aatagaaaaa 960
240 cagatgatcc agaacaaaaa gcaaaagtta agaaaaagaa gcctaaactt ttaaataaat 1020
241 ttgataagac tattaaagct gaacttgatg ctgcagaaaa actccgtaaa aggggaaaaa 1080
242 ttgaggaagc agtgaatgca tttaaagaac tagtacgcaa ataccctcag agtccacgag 1140
243 caagatatgg gaaggcgcag tgtgaggatg atttggctga gaagaggaga agtaatgagg 1200
244 tgctacgtgg agccatcgag acctaccaag aggtggccag cctacctgat gtccctgcag 1260
245 acctgctgaa gctgagtttg aagcgtcgct cagacaggca acaatttcta ggtcatatga 1320
246 gaggttccct gcttaccctg cagagattag ttcaactatt tcccaatgat acttccttaa 1380
247 aaaatgacct tggcgtggga tacctcttga taggagataa tgacaatgca aagaaagttt 1440
248 atgaagaggt gctgagtgtg acacctaatg atggctttgc taaagtccat tatggcttca 1500
249 tcctgaaggc acagaacaaa attgctgaga gcatcccata tttaaaggaa ggaatagaat 1560
250 ccggagatcc tggcactgat gatgggagat tttatttcca cctggggggat gccatgcaga 1620
251 gggttgggaa caaagaggca tataagtggt atgagcttgg cacaagaga ggacactttg 1680
252 catctgtctg gcaacgctca ctctacaatg tgaatggact gaaagcacag ccttggtgga 1740
253 ccccaaaaga aacgggctac acagagttag taaagtcttt agaaagaaac tggaagttaa 1800
254 tccgagatga aggccttgca gtgatggata aagccaaagg tctcttcctg cctgaggatg 1860
255 aaaacctgag ggaaaaaggg gactggagcc agttcacgct gtggcagcaa ggaagaagaa 1920
256 atgaaaatgc ctgcaaagga gctcctaaaa cctgtacctt actagaaaag ttccccgaga 1980
257 caacaggatg cagaagagga cagatcaaat attccatcat gcaccccggg actcacgtgt 2040
258 ggccgcacac agggcccaca aactgcaggc tccgaatgca cctgggcttg gtgattccca 2100
259 aggaaggctg caagattcga tgtgccaacg agaccaggac ctgggaggaa ggcaaggtgc 2160
260 tcatctttga tgactccttt gagcacgagg tatggcagga tgcctcatct ttccggctga 2220
261 tattcatcgt ggatgtgtgg catccggaac tgacaccaca gcagagacgc agccttccag 2280
262 caatttagca tgaattcatg caagcttggg aaactctgga gaga           2324
265 <210> SEQ ID NO: 4
266 <211> LENGTH: 31
267 <212> TYPE: PRT
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268 <213> ORGANISM: Artificial Sequence
270 <220> FEATURE:
271 <223> OTHER INFORMATION: Description of Artificial Sequence: EGF-like
272       cysteine-rich repeat
274 <220> FEATURE:
275 <221> NAME/KEY: VARIANT
276 <222> LOCATION: (3)..(5)
277 <223> OTHER INFORMATION: Wherein any Xaa may be any amino acid
279 <220> FEATURE:
280 <221> NAME/KEY: VARIANT
281 <222> LOCATION: (6)..(7)
282 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
284 <220> FEATURE:
285 <221> NAME/KEY: VARIANT
286 <222> LOCATION: (10)
287 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
289 <220> FEATURE:
290 <221> NAME/KEY: VARIANT
291 <222> LOCATION: (14)
292 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
294 <220> FEATURE:
295 <221> NAME/KEY: VARIANT
296 <222> LOCATION: (17)..(18)
298 <220> FEATURE:
299 <221> NAME/KEY: VARIANT
300 <222> LOCATION: (25)..(26)
301 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
303 <220> FEATURE:
304 <221> NAME/KEY: VARIANT
305 <222> LOCATION: (29)
306 <223> OTHER INFORMATION: Wherein Xaa is any amino acid.
308 <400> SEQUENCE: 4
309 Cys Asp Xaa Xaa Xaa Cys Xaa Xaa Lys Xaa Gly Asn Gly Xaa Cys Asp
310   1               5                   10                  15
312 Xaa Xaa Cys Asn Asn Ala Ala Cys Xaa Xaa Asp Gly Xaa Asp Cys
313               20                  25                  30
316 <210> SEQ ID NO: 5
317 <211> LENGTH: 1242
318 <212> TYPE: PRT
319 <213> ORGANISM: Homo sapiens
321 <400> SEQUENCE: 5
322 Met Ala Ser Pro Pro Glu Ser Asp Gly Phe Ser Asp Val Arg Lys Val
323   1               5                   10                  15
325 Gly Tyr Leu Arg Lys Pro Lys Ser Met His Lys Arg Phe Phe Val Leu
326               20                  25                  30
328 Arg Ala Ala Ser Glu Ala Gly Gly Pro Ala Arg Leu Glu Tyr Tyr Glu
329               35                  40                  45
331 Asn Glu Lys Lys Trp Arg His Lys Ser Ser Ala Pro Lys Arg Ser Ile
332           50                  55                  60
```

W--> 309
W--> 312

VERIFICATION SUMMARY   DATE: 10/30/2001
PATENT APPLICATION: US/09/903,248   TIME: 15:16:59

Input Set : A:\Rih32d51.app
Output Set: N:\CRF3\10302001\I903248.raw

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L:57 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1
L:60 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1
L:63 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1
L:309 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4
L:312 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4
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